## REMARKS/ARGUMENTS

By this Amendment, claim 19 is amended. Claims 12-18, 20 have been withdrawn from consideration pursuant to a restriction requirement. Claims 1-20 are pending.

Cancellation of and/or amendment to the claims should in no way be construed as an acquiescence to any of the Examiner's rejections. The cancellation and/or amendments to the claims are being made solely to expedite prosecution of the instant application.

Citations to the Specification are directed to U.S. Patent Application Publication No. 2005/0182114 (Parthasaradhi). Support for the amendment to claim 19 adding the limitation wherein the pharmaceutical composition is solid, can be found throughout the Specification as filed, and specifically in originally filed claim 10, and ¶[0019]

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Reconsideration of the restriction requirement is respectfully requested.

### Election/Restriction

Applicants hereby affirm their prior election with traverse of Group I, claims 1-11 and 19, reserving their rights under 35 USC § 121 to file a divisional application for the nonelected claims.

### Withdrawn Rejections

Applicant gratefully acknowledges the withdrawal of the rejection of claims 3 and 8 under 35 USC 112, second paragraph.

Applicant gratefully acknowledges the withdrawal of the rejection of claims 1-2 under 35 U.S.C. 103(a) over Naka et al. US 5,196,444 in view of Brittain's publication.

**Rejection under 35 USC 112, second paragraph**

Claims 4 and 9 stand rejected under 35 USC 112, second paragraph. This rejection is respectfully traversed.

The Examiner maintains the rejection allegedly because the X-ray powder diffraction data of Figure 1 or Figure 2 has not been incorporated into claims 4 and 9 respectively. However, incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." *Ex parte Fressola*, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993). MPEP 23173.05(s). Here, the claims are incorporating the X-ray powder diffraction pattern as set forth in Figures 1 and 2 because there is not a more concise way to incorporate the data from the X-ray powder diffraction pattern, other than to incorporate the Figures by reference. Since it would be unwieldy to duplicate the Figures into the claims, reconsideration and withdrawal of the rejection is respectfully requested.

**Rejection under 35 USC 112, first paragraph**

Claim 19 stands rejected under 35 U.S.C. 112, first paragraph as allegedly lacking enablement. This rejection is respectfully traversed.

The Examiner maintains the rejection allegedly because applicants do not provide direct evidence that the instant pharmaceutical compositions comprising candesartan cilexetil form III

are stable after the processes of preparing (i.e., i.e." mixing, grinding, and compressing, or converting into the instant form IV). Without acquiescing to the propriety of the Examiner's rejection, and solely in an effort to expedite prosecution, claim 19 has been amended herewith to recite a solid pharmaceutical composition.

Therefore, here the claim is enabled because there is not any reason to doubt the objective truth of the statements contained in the Specification for enabling support. The Specification discloses the manner and process for making and using the claimed invention, including examples which show the efficacy of the claimed invention. Applicants disclose a novel 1,4-dioxane solvate of candesartan cilexetil and two novel crystalline forms of candesartan cilexetil ¶[0004]. In Example 1, Applicants disclose a method of producing candesartan cilexetil solvate ¶[0019]. In Example 2, Applicants disclose a method of producing candesartan cilexetil form III ¶[0020]. In Example 4, Applicants disclose a method of producing candesartan cilexetil form IV ¶[0022].

Thus, given the teachings of the Specification, in light of the further experimentation carried out by the Applicant using the disclosed methods, the quantity of experimentation required is not excessive in view of the subject matter of the claims. The Specification sets forth several methods for producing the novel 1,4-dioxane solvate of candesartan cilexetil, and the two novel crystalline forms of candesartan cilexetil. Working Examples are also provided, as well as detailed information as to the methods. This information can be used by one of ordinary skill in the art to determine appropriate solution conditions make and use the claimed invention, without undue experimentation.

Accordingly, reconsideration and withdrawal of the rejection of pending claim 19 as lacking enablement is respectfully requested.

**Rejection under 35 USC 102(b)**

Claim 19 stands rejected under 35 U.S.C. 102(b) over Naka et al. US 5,196,444. This rejection is respectfully traversed.

The Examiner argues that an acceptable carrier can be water and therefore the instant crystal forms of the instant compound dissolves in the composition (i.e. aqueous solution), and it will exist in free form and not as a crystal form or a solvate form. The Examiner sets forth that amendment of claim 19 as a solid pharmaceutical composition would obviate the rejection.

Without acquiescing to the propriety of the Examiner's rejection, and solely in an effort to expedite prosecution, claim 19 has been amended herewith to recite a solid pharmaceutical composition. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

**Rejection under 35 USC 103(a)**

Claims 3-11, and 19 stand rejected under 35 USC 103(a) over Naka et al. US 5,196,444 in view of Brittain's publication. This rejection is respectfully traversed.

The Examiner argues that Naka et al. disclose crystalline form of the instant candesartan cilexetil compound, and alleges that since claims 3-11 and 19 are drawn to crystalline candesartan cilexetil compound/compositions and their processes.

However, the prior art relied upon by the Examiner does not teach or suggest the specific polymorphs as claimed by Applicant. The Examiner failed to demonstrate that the prior art even

recognized that the claimed compound exists in different polymorphic forms, or that there is a known or obvious way to manufacture the specific polymorphic form claimed. Here, the Examiner has assumed, without providing any evidence that the methods of producing candesartan cilexetil in the '444 Naka patent can be altered to produce the claimed polymorphs. However, there is no motivation for one of skill in the art to alter the methods of the '444 Naka patent to arrive at the claimed method, and no reasonable expectation of success. There is no teaching or suggestion within the Brittain references to alter the method as taught by the '444 Naka patent to arrive at the instantly claimed method. The Examiner argues that the motivation is that the skilled artisan would be motivated to employ the process taught by the '444 Naka patent to crystallize candesartan cilexetil and expect to obtain the desired product because he would have expected the analogous solvents and solute to behave similarly. However, the combination of the '444 Naka patent and the Brittain reference does not disclose or suggest methods of preparation of candesartan cilexetil crystalline forms wherein the solvent is 1,4-dioxane. Since the references do not disclose or suggest this, there is no motivation to employ the process taught by the '444 Naka patent or the Brittain reference to crystallize candesartan cilexetil and expect to obtain the desired product to reach the limitations of the claims, and no expectation of success.

Accordingly, reconsideration and withdrawal of the rejection of claims 3-11 and 19 under 35 USC 103(a) is respectfully requested.

**Rejection under 35 USC 103(a)**

Claims 1-11 and 19 stand rejected under 35 U.S.C. 103(a) as allegedly being obvious

over Naka et al. US 5,196,444 in view of publication of U.S. Department of Health and Human Service, Guidance for Industry, May 15, 2001. This rejection is respectfully traversed.

The claims are patentable over the combination of the Naka et al. US 5,196,444 and the U.S. Department of Health and Human Service, Guidance for Industry for the following reasons. The framework for the objective analysis for determining obviousness under 35 U.S.C. 103 is stated in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Obviousness is a question of law based on underlying factual inquiries. The factual inquiries enunciated by the Court are as follows: (A) Determining the scope and content of the prior art; and (B) Ascertaining the differences between the claimed invention and the prior art; and (C) Resolving the level of ordinary skill in the pertinent art. To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385 (CCPA 1970). MPEP 2143.03. It is important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. (*KSR v Teleflex*, 12 S.Ct. 1727, 1740 (US 2007)). Often, it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. (*Id.*).

The Examiner argues that Naka et al. discloses crystalline form of candesartan cilexetil

solvate (i.e., 1-(Cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-((2'-( 1 H-tetrazol-5-yl)biphenyl-4-yl)methyl)benzimidazole-7-carboxylate or its solvate or solvent form). The Examiner admits that Naka et al. is silent on the X-ray diffraction data of the compound, and that Naka et al. is silent on the solvent 1,4-dioxane. The Examiner argues that Guidance for Industry, a publication of U.S. Department of Health and Human Service, discloses 1,4-doxane is suitable pharmaceutical solvent for a pharmaceutical compound.

However, the instant claims are directed to a novel 1,4-dioxane solvate of candesartan cilexetil and two novel crystalline forms of candesartan cilexetil. The prior art relied upon by the Examiner does not teach or suggest the specific polymorphs as claimed by Applicant. The Examiner failed to demonstrate that the prior art even recognized that the claimed compound exists in different polymorphic forms, or that there is a known or obvious way to manufacture the specific polymorphic form claimed. Here, the Examiner has assumed, without providing any evidence that the methods of producing candesartan cilexetil in the '444 Naka patent can be altered to produce the claimed polymorphs.

The Examiner cites the Guidance for Industry publication as allegedly teaching the use of 1,4-dioxane solvent with a pharmaceutical compound. However, the Guidance for Industry is silent with regard to the compound candesartan cilexetil. The Examiner argues that it is obvious to try different solvents as listed in Table 2 of the Guidance for Industry document, with any pharmaceutical compound. However, an "obvious to try" rationale may support a conclusion that a claim would have been obvious where one skilled in the art is choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success. "[A] person

of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely that product [was] not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1397 (2007). Here, there was no reasonable expectation of success in combining the Naka patent with the Guidance for Industry publication because as the Guidance for Industry reference teaches, the solvents in Table 2 should be limited in pharmaceutical products because of their inherent toxicity. Therefore, the Guidance for Industry teaches away from the use of 1,4-dioxane. It is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983), MPEP 2145.

Accordingly, reconsideration and withdrawal of the rejection of claims 1-11 and 19 under 35 USC 103(a) is respectfully requested.

**Claim Objection**

Claim 6 is objected to as depending on a non-elected subjected matter (i.e. amorphous form). Without acquiescing to the propriety of the Examiner's objection, and solely in an effort to expedite prosecution, claim 6 has been amended to remove the reference to the amorphous form. Reconsideration and withdrawal of the objection is respectfully requested.

* * *

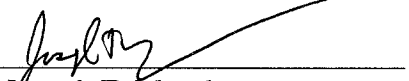
For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

Should the Examiner believe that anything further is desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

CAESAR, RIVISE, BERNSTEIN,
COHEN & POKOTILOW, LTD.

March 26, 2008

By 

Joseph F. Murphy
Registration No. 58,313
Customer No. 03000
(215) 567-2010
Attorneys for Applicants

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